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TITLE: Randomized Phase II Trial of Adjuvant WT-1 Analog Peptide Vaccine in Patients with Malignant Pleural Mesothelioma after Completion of Multimodality Therapy

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14. ABSTRACT

The Wilms' tumor gene, WT1, encodes transcription factors that regulate cell proliferation, differentiation, and apoptosis. WT1 protein is highly expressed in malignant pleural mesothelioma (MPM), and is a rational target for immunotherapy. We have developed a vaccine comprised of four WT1 heteroclitic peptides that are given together with Montanide and GM-CSF as immunologic adjuvants. This WT1 vaccine was previously tested in a small pilot trial, and shown to be safe and immunogenic. We have chosen to test the efficacy of this vaccine in MPM patients who have minimal disease burden after completion of multimodality therapy, but remain at exceedingly high risk for recurrence. The specific aim of this project is to conduct a multicenter, blinded, randomized trial comparing treatment with the WT-1 peptide vaccine + Montanide/GM-CSF to treatment with Montanide/GM-CSF alone in patients with MPM who have completed multimodality therapy. The primary endpoint is progression free survival. The trial has opened at Memorial Sloan-Kettering and is actively enrolling patients.

15. SUBJECT TERMS
Mesothelioma, WT1, vaccine

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INTRODUCTION:

The Wilms' tumor gene, WT1, encodes transcription factors that regulate cell proliferation, differentiation, and apoptosis. WT1 protein is highly expressed in malignant pleural mesothelioma (MPM), and is a rational target for immunotherapy. We have developed a vaccine comprised of four WT1 heteroclitic peptides that are given together with Montanide and GM-CSF as immunologic adjuvants. This WT1 vaccine was previously tested in a small pilot trial, and shown to be safe and immunogenic. We have chosen to test the efficacy of this vaccine in MPM patients who have minimal disease burden after completion of multimodality therapy, but remain at exceedingly high risk for recurrence. The specific aim of this project is to conduct a multicenter, double-blinded, randomized trial comparing treatment with the WT-1 peptide vaccine + Montanide/GM-CSF to treatment with Montanide/GM-CSF alone in patients with MPM who have completed multimodality therapy. The primary endpoint is progression free survival.

BODY:

This project has proceeded as indicated in the approved Statement of Work:

- The peptides were purchased, manufactured, and underwent sterility testing.
    - The peptides were ordered from AmbioPharm, Inc. Once produced, they were vialed under GMP conditions by University of Iowa Pharmaceuticals. The investigational agent completed sterility and stability testing to ensure safety for human use. The vials were delivered to the pharmacy at MSKCC.
- The protocol was reviewed by the various committees at MSKCC and the DOD leading to IRB approval.
    - After IRB approval in September, 2010, the study received approval from the FDA on 12/21/2010. During that time, the protocol was reviewed by the HRPO at the Department of Defense and several comments were made requiring changes to the protocol. The requested changes were made, reviewed by HRPO, and an amendment to the protocol was submitted to the IRB. The amendment was approved on 2/9/11. Final review took place by HRPO and an approval memo was issued on 2/11/11.
    - A start-up meeting was held with the research staff on 2/1/11 to inform all of the participants about the rationale, design, and logistics of this study.
- M.D Anderson Cancer Center received IRB approval for the protocol in August, 2012, but they were unable to enroll their first patient until April, 2013 due to delays related to institutional processes, and FDA and DOD approvals.
- Additional sites have not yet been recruited for participation in the study due to budget constraints.

KEY RESEARCH ACCOMPLISHMENTS:

- The planned randomized phase II trial is open at MSKCC and MDACC and is actively accruing patients. 21 patients have been enrolled including 18 from MSKCC and 3 from MDACC. No treatment related adverse events have occurred.

REPORTABLE OUTCOMES:

This protocol was highlighted in several presentations which have increased exposure and enrollment. This includes:
ASCO 2011, Chicago, IL - poster presented at Trials in Progress Session
World Conference on Lung Cancer, Amsterdam, Jul 2011, slide presentation
Meso Foundation Symposium Jul 2011 and Jul 2012, Washington DC
http://www.youtube.com/watch?v=VNUXss6B2uY
Meso Foundation Podcast, Feb 23, 2012.

CONCLUSION:

The clinical trial is open to enrollment at Memorial Sloan-Kettering and MD Anderson which will continue for the next two years. The rate of accrual is slower than expected due to the delays in getting MD Anderson open. As such, modifications to the study design and biostatistics will be explored.

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APPENDICES:

None

SUPPORTING DATA:

None